F ENT COOPERATION TREA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 05 November 1999 (05.11.99)	
International application No. PCT/AU99/00288	**Applicant's or agent's file reference**
International filing date (day/month/year) 16 April 1999 (16.04.99)	**Priority date** (day/month/year) 16 April 1998 (16.04.98)
Applicant DRINKWATER, Roger, Desmond et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

19 October 1999 (19.10.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
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1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Lazar Joseph Panakal

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2171650/MJC:/wm	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International application No. **PCT/AU99/00288**	International filing date *(day/month/year)* 16 April 1999	Priority Date *(day/month/year)* 16 April 1998
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] C07K 14/435, 16/18; A61K 38/17; C12N 15/12		
Applicant THE UNIVERSITY OF QUEENSLAND et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of **6** sheet(s).

3. This report contains indications relating to the following items:

I	[X]	Basis of the report
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[ ]	Certain observations on the international application

Date of submission of the demand 19 October 1999	Date of completion of the report 28 February 2000
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **CHRISTINE BREMERS** Telephone No. (02) 6283 2313

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU99/00288

I. Basis of the report

1. With regard to the **elements** of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages **1A-43**, as originally filed,
  pages , filed with the demand,
  pages , filed with the letter of .
- [X] the claims, pages , as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages **44-49**, filed with the letter of **17 February 2000**.
- [X] the drawings, pages **1/1**, as originally filed,
  pages , filed with the demand,
  pages , filed with the letter of .
- [X] the sequence listing part of the description:
  pages **1-27**, as originally filed
  pages , filed with the demand
  pages , filed with the letter of .

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:

- [X] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-19	**YES**
	Claims	**NO**
Inventive step (IS)	Claims 1-19	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims 1-19	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

Novelty and Inventive Step

D1 US 5424218
D2 Journal of Molecular Biology
D3 FEBS Letters

Documents D1-D3 disclose ω-conotoxin peptides with a sequence in the fourth loop between cysteine residues 5 and 6. However, the sequences in D1-D3 differ from SEQ.ID.No:1 of the claims.

Thus, claims 1-19 are considered novel and inventive.

THE CLAIMS:

1. An isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

2. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 in which the fourth loop consists of the sequence:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

3. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 or claim 2 wherein each of the first, second and third loops of the ω-conotoxin peptide corresponds to the loop of a naturally occurring ω-conotoxin peptide, or such a sequence of amino acids which has undergone one or more amino acid substitutions, additions or deletions.

4. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 wherein the second loop is selected from:

SKLMYD	[SEQ ID NO: 2],
SRLMYD	[SEQ ID NO: 3],
DRLMYD	[SEQ ID NO: 4],
DKLMYD	[SEQ ID NO: 33],
SKLAYD	[SEQ ID NO: 34],
SKLNleYD	[SEQ ID NO: 35],
SRLNleYD	[SEQ ID NO: 36],
SKLOhmhserYD	[SEQ ID NO: 37],
SKLOmserYD	[SEQ ID NO: 38],

5. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 having the following sequence:

CKSKGAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 5]
CKSKGAKCSRLMYDCCSGSCSGTVGRC	[SEQ ID NO: 6]
CKSKGAKCDRLMYDCCSGSCSGTVGRC	[SEQ ID NO: 7]
CRSKGAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 14]
CKSKGARCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 15]
CKSKGAQCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 16]
CKSKGAKCSKLMYDCCSGSCSGAVGRC	[SEQ ID NO: 17]
CKSKGAKCDKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 18]
CKYKGAKCSRLMYDCCSGSCSGTVGRC	[SEQ ID NO: 19]
CKSKGAKCSKLAYDCCSGSCSGTVGRC	[SEQ ID NO: 20]
CKSKGAKCSKLMYDCCTGSCSGTVGRC	[SEQ ID NO: 21]
CKSKDalAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 22]
CKSKGAKCSKLMYDCCSGSCSGTVGRCY	[SEQ ID NO: 23]
CKSKGAKCSKLMYDCCSGSCSGTVGRC-OH	[SEQ ID NO: 24]
YCKSKGAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 25]
Ac-CKSKGAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 26]

CKSKGAKCSKLNleYDCCSGSCSGTVGRC [SEQ ID NO: 27]
CKSKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 28]
CKYKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 29]
CKSKGAKCSKLOmhserYDCCSGSCSGTVGRC [SEQ ID NO: 30]
CKSKGAKCSKLOmserYDCCSGSCSGTVGRC [SEQ ID NO: 31]
CKSKGAKCSKLM(O)YDCCSGSCSGTVGRC [SEQ ID NO: 32]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

6. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 5 having one of the following sequences:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5]
CRSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 14]
CKSKGARCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 15]
CKSKGAKCSKLAYDCCSGSCSGTVGRC [SEQ ID NO: 20]
CKSKGAKCSKLNleYDCCSGSCSGTVGRC [SEQ ID NO: 27]
CKSKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 28]
CKSKGAKCSKLOmhserYDCCSGSCSGTVGRC [SEQ ID NO: 30]
CKSKGAKCSKLOmserYDCCSGSCSGTVGRC [SEQ ID NO: 31].

7. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 having the following sequence:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5].

8. An isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims having a selectivity for N-type calcium channels over P/Q-

type calcium channels.

9. Use of an isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims in a receptor binding assay to test the calcium channel binding activity of a peptide or other compound.

10. An isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a ω-conotoxin peptide according to any one of claims 1 to 8.

11. A nucleic acid probe comprising a sequence of nucleotides encoding or complementary to a sequence encoding all or part of an ω-conotoxin peptide according to any one of claims 1 to 8, said probe encoding or complementary to all or part of the fourth loop of said ω-conotoxin peptide.

12. A monoclonal or polyclonal antibody to an ω-conotoxin peptide according to any one of claims 1 to 8.

13. A genetic construct comprising a vector portion and a nucleic acid capable of encoding a peptide according to any one of claims 1 to 8.

14. A composition comprising: an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions, and

a pharmaceutically acceptable carrier or diluent.

15. Use of an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications in the manufacture of a medicament for the treatment of a condition where blockade of N-type calcium channels is associated with effective treatment.

16. Use of an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications in the manufacture of a medicament for the reduction of neuronal damage following ischemia, production of analgesia, enhancement of opiate analgesia, treatment of schizophrenia or the treatment of stimulant psychoses, hypertension, inflammation, diseases which cause bronchoconstriction or for inhibition of progression of neuropathic pain.

17. A method for the treatment of conditions for which blockade of N-type calcium channels is associated with effective treatment including the step of administering to a mammal an effective amount of an isolated or recombinant ω-conotoxin

peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

18. A method for reducing neuronal damage following ischemia, for the production of analgesia, for enhancement of opiate analgesia, for the treatment of schizophrenia, hypertension, inflammation or diseases which cause bronchoconstriction, stimulant psychoses or for inhibition of progression of neuropathic pain including the step of administering to a mammal an effective amount of an isolated or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

19. Use of an isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims in a screen to identify compounds with activity at N-type VSCCs.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/AU 99/00288	International filing date *(day/month/year)* 16 April 1999	(Earliest) Priority Date *(day/month/year)* 16 April 1998

Applicant
The University of Queensland et al.

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

[X] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

Novel omega conotoxin peptides.

5. With regard to the **abstract**,

[ ] the text is approved as submitted by the applicant

[X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure

[ ] because this figure better characterizes the invention

[ ] None of the figures

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

An isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises SEQ ID NO: 1 or such a sequence which has undergone one or more amino acid substitutions or side chain modifications, and uses therefore. SEQ ID NO: 1 comprises the amino acid sequence SGTVGR.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 99/00288

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: C07K 14/435, 16/18; A61K 38/17; C12N 15/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPIDS: cone shell or conotoxin or cone snail or conus. CA/medline: conotoxin, cone snail, conus, omega, calcium, channel, loop. STN subsequence and ANGIS: CSG[AT]VGRC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5424218 A (G.P. Miljanich et al) 13 June 1995 See claims and figures 1 and 2	1-3, 5-7, 9-20
X	Journal of Molecular Biology (1996) 263, 297-310, K.J. Nielsen et al. "A Consensus Structure for ω-Conotoxins with Different Selectivities for Voltage-sensitive Calcium Channel Subtypes: Comparison of MVIIA, SVIB and SNX-202.	1-3, 5-7, 9-14, 20.
X	FEBS Letters(1997) 414, 480-484, K. Sato et al. "Binding of Chimeric Analogs of ω-Conotoxin MVIIA and MVIIC to the N- and P/Q-type Calcium Channels."	1-3, 5-7, 9-14, 20.

☐ Further documents are listed in the continuation of Box C

☒ See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
11 May 1999

Date of mailing of the international search report
13 MAY 1999

Name and mailing address of the ISA/AU
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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/AU 99/00288

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Member					
US 5424218	AT 140388	AU 69640/91	AU 30745/92	CA 2045473	DE 69027865	EP 593450
	EP 557452	ES 2091906	JP 5501715	JP 6504642	WO 9107980	WO 920907
	WO 9310145	US 5189020	US 5264371	US 5559095	US 5303095	

END OF ANNEX

THE CLAIMS:

1. An isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

2. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 in which the fourth loop consists of the sequence:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

3. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 or claim 2 wherein each of the first, second and third loops of the ω-conotoxin peptide corresponds to the loop of a naturally occurring ω-conotoxin peptide, or such a sequence of amino acids which has undergone one or more amino acid substitutions, additions or deletions.

4. An isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims wherein said amino acid substitutions are conservative.

5. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1

wherein the second loop is selected from:

SKLMYD	[SEQ ID NO: 2],
SRLMYD	[SEQ ID NO: 3],
DRLMYD	[SEQ ID NO: 4],
DKLMYD	[SEQ ID NO: 33],
SKLAYD	[SEQ ID NO: 34],
SKLNleYD	[SEQ ID NO: 35],
SRLNleYD	[SEQ ID NO: 36],
SKLOhmhserYD	[SEQ ID NO: 37],
SKLOmserYD	[SEQ ID NO: 38].

6. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 6 having the following sequence:

CKSKGAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 5]
CKSKGAKCSRLMYDCCSGSCSGTVGRC	[SEQ ID NO: 6]
CKSKGAKCDRLMYDCCSGSCSGTVGRC	[SEQ ID NO: 7]
CRSKGAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 14]
CKSKGARCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 15]
CKSKGAQCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 16]
CKSKGAKCSKLMYDCCSGSCSGAVGRC	[SEQ ID NO: 17]
CKSKGAKCDKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 18]
CKYKGAKCSRLMYDCCSGSCSGTVGRC	[SEQ ID NO: 19]
CKSKGAKCSKLAYDCCSGSCSGTVGRC	[SEQ ID NO: 20]
CKSKGAKCSKLMYDCCTGSCSGTVGRC	[SEQ ID NO: 21]
CKSKDalAKCSKLMYDCCSGSCSGTVGRC	[SEQ ID NO: 22]
CKSKGAKCSKLMYDCCSGSCSGTVGRCY	[SEQ ID NO: 23]
CKSKGAKCSKLMYDCCSGSCSGTVGRC-OH	[SEQ ID NO: 24]

YCKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 25]
Ac-CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 26]
CKSKGAKCSKLNleYDCCSGSCSGTVGRC [SEQ ID NO: 27]
CKSKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 28]
CKYKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 29]
CKSKGAKCSKLOmhserYDCCSGSCSGTVGRC [SEQ ID NO: 30]
CKSKGAKCSKLOmserYDCCSGSCSGTVGRC [SEQ ID NO: 31]
CKSKGAKCSKLM(O)YDCCSGSCSGTVGRC [SEQ ID NO: 32]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

7. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 6 having one of the following sequences:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5]
CRSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 14]
CKSKGARCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 15]
CKSKGAKCSKLAYDCCSGSCSGTVGRC [SEQ ID NO: 20]
CKSKGAKCSKLNleYDCCSGSCSGTVGRC [SEQ ID NO: 27]
CKSKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 28]
CKSKGAKCSKLOmhserYDCCSGSCSGTVGRC [SEQ ID NO: 30]
CKSKGAKCSKLOmserYDCCSGSCSGTVGRC [SEQ ID NO: 31].

8. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 having the following sequence:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5].

9. An isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims having a selectivity for N-type calcium channels over P/Q-type calcium channels.

10. Use of an isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims in a receptor binding assay to test the calcium channel binding activity of a peptide or other compound.

11. An isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a ω-conotoxin peptide according to any one of claims 1 to 9.

12. A nucleic acid probe comprising a sequence of nucleotides encoding or complementary to a sequence encoding all or part of an ω-conotoxin peptide according to any one of claims 1 to 9, said probe encoding or complementary to all or part of the fourth loop of said ω-conotoxin peptide.

13. A monoclonal or polyclonal antibody to an ω-conotoxin peptide according to any one of claims 1 to 9.

14. A genetic construct comprising a vector portion and a nucleic acid capable of encoding a peptide according to any one of claims 1 to 9.

15. A composition comprising: an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions, and

a pharmaceutically acceptable carrier or diluent.

16. Use of an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications in the manufacture of a medicament for the treatment of a condition where blockade of N-type calcium channels is associated with effective treatment.

17. Use of an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications in the manufacture of a medicament for the reduction of neuronal damage following ischemia, production of analgesia, enhancement of opiate analgesia, treatment of schizophrenia or the treatment of stimulant psychoses, hypertension, inflammation, diseases which cause bronchoconstriction or for inhibition of progression of neuropathic pain.

18. A method for the treatment of conditions for which blockade of N-type calcium channels is associated with effective treatment including the step of administering to a mammal an effective amount of an isolated or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

19. A method for reducing neuronal damage following ischemia, for the production of analgesia, for enhancement of opiate analgesia, for the treatment of schizophrenia, hypertension, inflammation or diseases which cause bronchoconstriction, stimulant psychoses or for inhibition of progression of neuropathic pain including the step of administering to a mammal an effective amount of an isolated or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

20. Use of an isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims in a screen to identify compounds with activity at N-type VSCCs.

THE CLAIMS:

1. An isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

2. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 in which the fourth loop consists of the sequence:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

3. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 or claim 2 wherein each of the first, second and third loops of the ω-conotoxin peptide corresponds to the loop of a naturally occurring ω-conotoxin peptide, or such a sequence of amino acids which has undergone one or more amino acid substitutions, additions or deletions.

4. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 wherein the second loop is selected from:

SKLMYD [SEQ ID NO: 2],
SRLMYD [SEQ ID NO: 3],
DRLMYD [SEQ ID NO: 4],
DKLMYD [SEQ ID NO: 33],
SKLAYD [SEQ ID NO: 34],
SKLNleYD [SEQ ID NO: 35],
SRLNleYD [SEQ ID NO: 36],
SKLOhmhserYD [SEQ ID NO: 37],
SKLOmserYD [SEQ ID NO: 38],

5. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 having the following sequence:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5]
CKSKGAKCSRLMYDCCSGSCSGTVGRC [SEQ ID NO: 6]
CKSKGAKCDRLMYDCCSGSCSGTVGRC [SEQ ID NO: 7]
CRSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 14]
CKSKGARCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 15]
CKSKGAQCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 16]
CKSKGAKCSKLMYDCCSGSCSGAVGRC [SEQ ID NO: 17]
CKSKGAKCDKLMYDCCSGSCSGTVGRC [SEQ ID NO: 18]
CKYKGAKCSRLMYDCCSGSCSGTVGRC [SEQ ID NO: 19]
CKSKGAKCSKLAYDCCSGSCSGTVGRC [SEQ ID NO: 20]
CKSKGAKCSKLMYDCCTGSCSGTVGRC [SEQ ID NO: 21]
CKSKDalAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 22]
CKSKGAKCSKLMYDCCSGSCSGTVGRCY [SEQ ID NO: 23]
CKSKGAKCSKLMYDCCSGSCSGTVGRC-OH [SEQ ID NO: 24]
YCKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 25]
Ac-CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 26]

CKSKGAKCSKLNleYDCCSGSCSGTVGRC [SEQ ID NO: 27]
CKSKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 28]
CKYKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 29]
CKSKGAKCSKLOmhserYDCCSGSCSGTVGRC [SEQ ID NO: 30]
CKSKGAKCSKLOmserYDCCSGSCSGTVGRC [SEQ ID NO: 31]
CKSKGAKCSKLM(O)YDCCSGSCSGTVGRC [SEQ ID NO: 32]

or such a sequence which has undergone one or more amino acid substitutions or side chain modifications.

6. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 5 having one of the following sequences:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5]
CRSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 14]
CKSKGARCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 15]
CKSKGAKCSKLAYDCCSGSCSGTVGRC [SEQ ID NO: 20]
CKSKGAKCSKLNleYDCCSGSCSGTVGRC [SEQ ID NO: 27]
CKSKGAKCSRLNleYDCCSGSCSGTVGRC [SEQ ID NO: 28]
CKSKGAKCSKLOmhserYDCCSGSCSGTVGRC [SEQ ID NO: 30]
CKSKGAKCSKLOmserYDCCSGSCSGTVGRC [SEQ ID NO: 31].

7. An isolated, synthetic or recombinant ω-conotoxin peptide according to claim 1 having the following sequence:

CKSKGAKCSKLMYDCCSGSCSGTVGRC [SEQ ID NO: 5].

8. An isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims having a selectivity for N-type calcium channels over P/Q-

type calcium channels.

9. Use of an isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims in a receptor binding assay to test the calcium channel binding activity of a peptide or other compound.

10. An isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a ω-conotoxin peptide according to any one of claims 1 to 8.

11. A nucleic acid probe comprising a sequence of nucleotides encoding or complementary to a sequence encoding all or part of an ω-conotoxin peptide according to any one of claims 1 to 8, said probe encoding or complementary to all or part of the fourth loop of said ω-conotoxin peptide.

12. A monoclonal or polyclonal antibody to an ω-conotoxin peptide according to any one of claims 1 to 8.

13. A genetic construct comprising a vector portion and a nucleic acid capable of encoding a peptide according to any one of claims 1 to 8.

14. A composition comprising: an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions, and

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a pharmaceutically acceptable carrier or diluent.

15. Use of an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications in the manufacture of a medicament for the treatment of a condition where blockade of N-type calcium channels is associated with effective treatment.

16. Use of an isolated, synthetic or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications in the manufacture of a medicament for the reduction of neuronal damage following ischemia, production of analgesia, enhancement of opiate analgesia, treatment of schizophrenia or the treatment of stimulant psychoses, hypertension, inflammation, diseases which cause bronchoconstriction or for inhibition of progression of neuropathic pain.

17. A method for the treatment of conditions for which blockade of N-type calcium channels is associated with effective treatment including the step of administering to a mammal an effective amount of an isolated or recombinant ω-conotoxin

peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

18. A method for reducing neuronal damage following ischemia, for the production of analgesia, for enhancement of opiate analgesia, for the treatment of schizophrenia, hypertension, inflammation or diseases which cause bronchoconstriction, stimulant psychoses or for inhibition of progression of neuropathic pain including the step of administering to a mammal an effective amount of an isolated or recombinant ω-conotoxin peptide in which the fourth loop between cysteine residues 5 and 6 comprises the following sequence of amino acids:

SGTVGR [SEQ ID NO: 1]

or such a sequence which has undergone one or more conservative amino acid substitutions or side chain modifications.

19. Use of an isolated, synthetic or recombinant ω-conotoxin peptide according to any one of the preceding claims in a screen to identify compounds with activity at N-type VSCCs.

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2171650/MJC:/wm	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International application No. **PCT/AU99/00288**	International filing date *(day/month/year)* 16 April 1999	Priority Date *(day/month/year)* 16 April 1998
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] C07K 14/435, 16/18; A61K 38/17; C12N 15/12		
Applicant THE UNIVERSITY OF QUEENSLAND et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheet(s).

3. This report contains indications relating to the following items:

I	[X]	Basis of the report
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[ ]	Certain observations on the international application

Date of submission of the demand 19 October 1999	Date of completion of the report 28 February 2000
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **CHRISTINE BREMERS** Telephone No. (02) 6283 2313

INTERNATIONAL PRE[redacted]NARY EXAMINATION REPORT

International application No.
[redacted]T/AU99/00288

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed.

☒ the description, pages **1A-43**, as originally filed,
pages , filed with the demand,
pages , filed with the letter of .

☒ the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages **44-49**, filed with the letter of **17 February 2000**.

☒ the drawings, pages **1/1**, as originally filed,
pages , filed with the demand,
pages , filed with the letter of .

☒ the sequence listing part of the description:
pages **1-27**, as originally filed
pages , filed with the demand
pages , filed with the letter of .

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-19	YES
	Claims	NO
Inventive step (IS)	Claims 1-19	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-19	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)

Novelty and Inventive Step

D1 US 5424218
D2 Journal of Molecular Biology
D3 FEBS Letters

Documents D1-D3 disclose ω-conotoxin peptides with a sequence in the fourth loop between cysteine residues 5 and 6. However, the sequences in D1-D3 differ from SEQ.ID.No:1 of the claims.

Thus, claims 1-19 are considered novel and inventive.